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TUBERCULOUS ABSCESSES OF THE BRAIN SECONDARY TO TUBERCULOSIS OF THE CÆCUM

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THE central nervous system is not infrequently invaded by tuberculosis. This invasion usually occurs as tuberculous meningitis, miliary tuberculosis, or less frequently as single or multiple tuberculomata. Tubercle or tuberculoma formations may become confluent and involve relatively large areas of the brain, caseation and breaking down of tissue with secondary infection resulting. On the other hand, true tuberculous abscesses of the brain are very rare. Their pathology differs from that of tuberculous abscesses elsewhere in the body in that it does not involve the various stages of granulomatous change to be expected from an infecting organism of this nature. Apparently these abscesses are blood-borne infections from a chronic tuberculous process elsewhere in the body. The method of abscess formation resembles that of other cerebral abscesses caused by pyogenic infecting organisms when these are blood-borne. There is probably a primary period of localized encephalitis, a secondary period of softening, and a final period of capsule formation, in the development of a true abscess. The case here reported is of such a type.

CASE REPORT

Tuberculous abscess of the cerebellum and right frontal lobe, complicating a tuberculoma of the cæcum, in a Japanese 46 years old.

M. Y., Japanese male, fish merchant, aged 46 years and single, referred by Dr. K. Tashiro, of Los Angeles, on October 23, 1933, for symptoms resembling those of a tumor of the brain. He was born in Japan, coming to this country at the age of 18. He is said to have had an attack of acute appendicitis in 1925 for which he was not operated upon. He was a heavy smoker and drinker. There was no history of chronic cough, chills, fever, expectoration, or loss of weight. On May 12, 1932, he was examined by Dr. Walter Wessels of Los Angeles, who obtained a history that during the previous 2½ months he had developed slight pain in the abdomen morning and evening. A month prior to Dr. Wessel's examination he had had an attack of colic which lasted 1 day; this was followed by constipation which was relieved by taking some "gas powders." There had never been any nausea or vomiting.

His physical examination was entirely negative except for 3 devitalized teeth, a slightly enlarged heart and a tumor mass in the right lower quadrant. This mass was described as being about the size of a lemon, rather hard, freely movable, smooth, occupying a position 3 centimeters to the right of the umbilicus and extending from the level of the umbilicus downward for 5 centimeters. The right kidney could be felt above and was distinct from the mass. A gastro-intestinal study was negative except that the ascending transverse and descending colon was found to be narrow and spastic. The ascending colon was interfered with by the palpable mass which moved with it upon manipulation. The cæcum was filled. The bowel appeared to be pushed to the extreme right. No appendix was seen. The blood Wassermann was negative. Urinalysis and examination of the stool were negative. Blood count: hæmoglobin 80 per cent, red blood cells 4,480,000, white blood cells 14,000, differential: lymphocytes 26 per cent, polymorphonuclears 57 per cent, large lymphocytes 9 per cent, mononuclears 5 per cent, eosinophils 3 per cent. The diagnosis at that time seemed to rest between: (a) perityphlitis, (b) Meckel's diverticulum, (c) omental cyst, (d) hydatid cyst, and (e) carcinoma of the cæcum. An exploratory laparotomy was recommended but was not carried out.

When first seen by me on October 22, 1933, a different picture presented. There was a large movable tumor in the right lower quadrant of the abdomen which was not painful or tender on pressure but which was now about the size of a man's fist. The patient gave a history also of periodical attacks of partial intestinal obstruction. Roentgenological studies following a barium meal test showed a marked filling defect in the region of the cæcum.

There was a further history of headaches dating back about 4 weeks. The pain was most marked in the right suboccipital region. There had been a great deal of nausea and frequent vomiting. The patient had lost weight. He had been unsteady on his feet and apparently very ataxic. He preferred to lie on the right side, becoming very dizzy if he turned to the left side. One made out no evidence of tuberculosis in the chest. The sense of smell was present on the right side but lost on the left side. His discs showed no choking. There was a slight horizontal nystagmus on looking to the right, none on looking to the left. There was slight weakness of the right lower face. The Romberg symptom and gait could not be tested, but when propped up in bed the patient fell backward and to the right. There were no abnormal reflexes of the Babinski group on either side. No ankle clonus was present. Blood Wassermann was again negative. A spinal fluid examination showed a clear fluid, containing one cell, marked increase in globulin, negative Wassermann. Colloidal gold curve 0000000000. No tubercle bacilli or other organisms were seen.

The presence of an expanding lesion in the right cerebellar lobe was suspected. The question arose as to whether this was secondary to the tumor in the abdomen and an exploratory laparotomy was suggested.

On October 28, 1933, the patient was operated upon by Dr. K. Tashiro. At operation the mass proved to be an extensive tubercular lesion involving a very movable cæcum and the adjacent terminal ileum, with regional mesenteric and omental changes. The cæcum and lower portion of the ascending colon were quite thickened and moderately indurated as was also a portion of the terminal ileum about 3 inches long. The appendix was retrocæcal and bound down in a mass of adhesions. An extensive resection of the cæcum and ascending colon as high as the hypatic flexure and also including 6 inches of the terminal ileum was carried out. An isoperistaltic side-to-side bowel anastomosis was then done, uniting the transverse colon to the terminal ileum. The wound was drained with a cigarette

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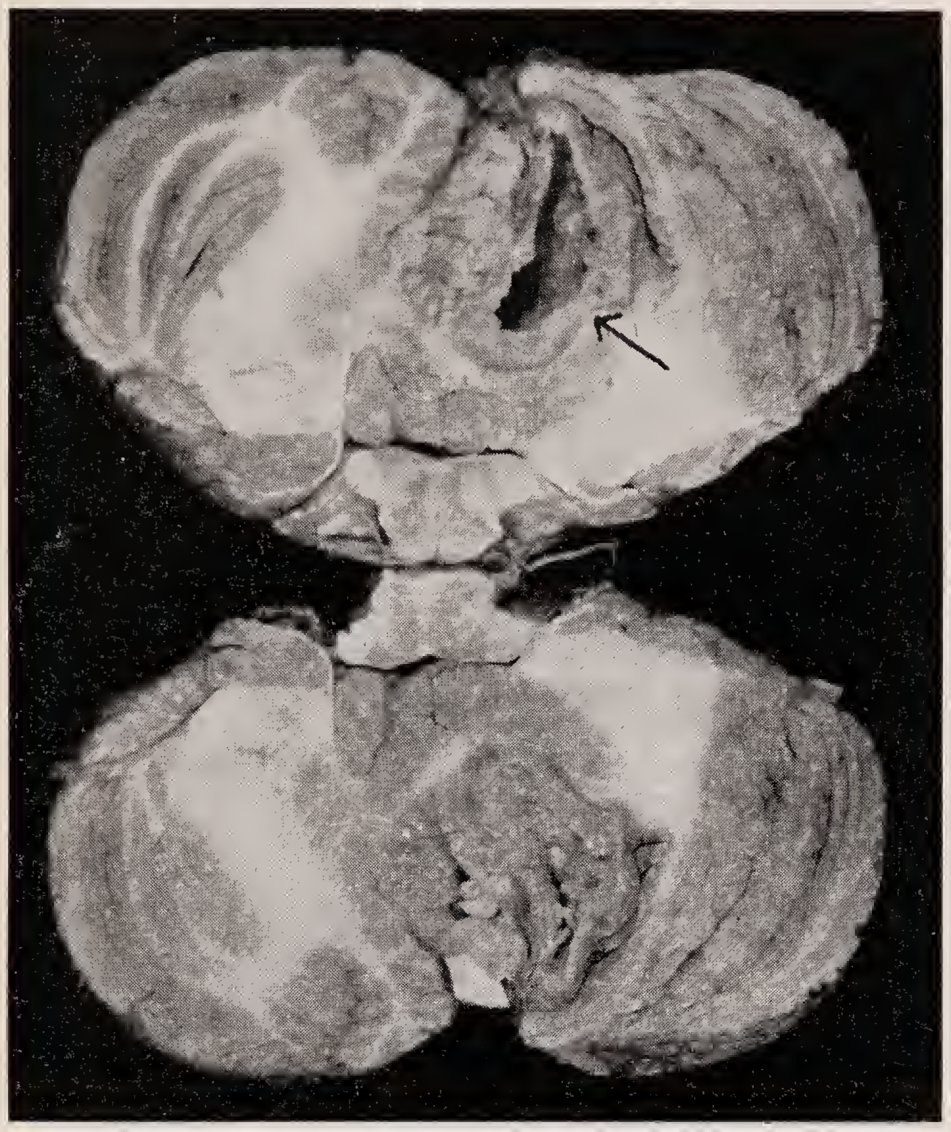

Fig. 1. Cerebellum cut in horizontal plane to show tuberculous abscess in cerebellar lobe adjacent to vermis.

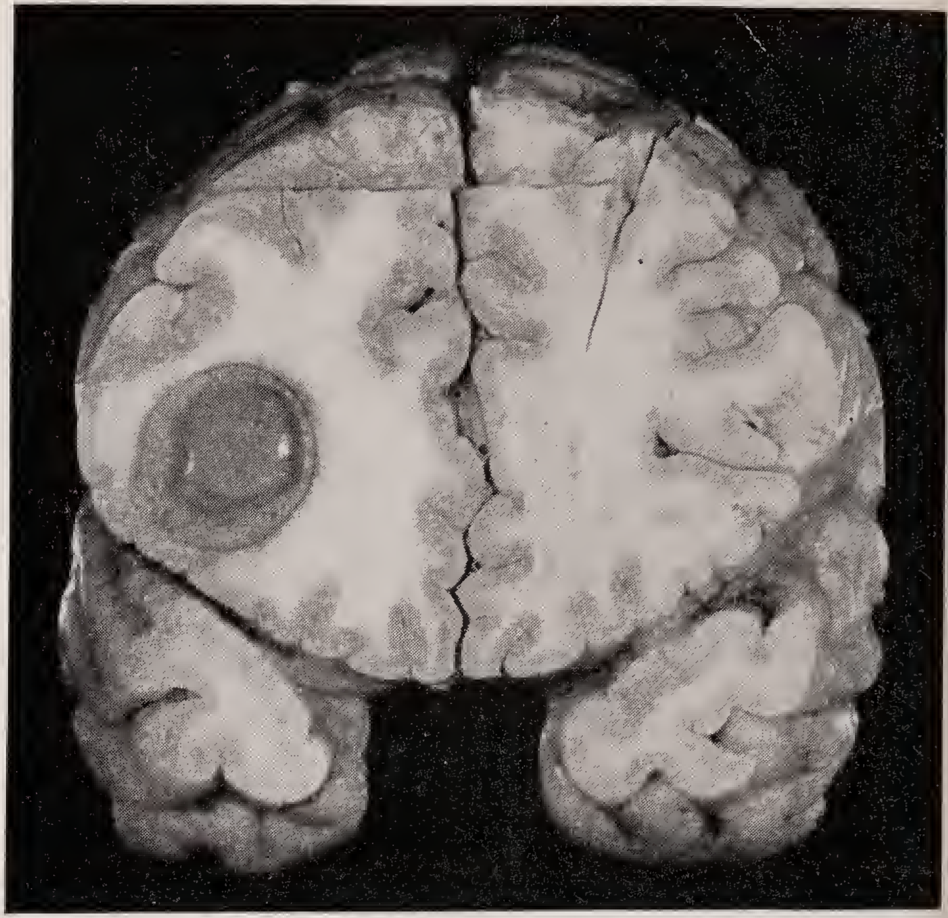

Fig. 2. Coronal section of brain showing tuberculous abscess in right frontal lobe. Note the discrete capsule and absence of gross inflammatory changes about the abscess.

drain and then closed. Following this, so far as abdominal symptoms were concerned, the patient made an uneventful convalescence. The wound healed *per primam* and free bowel action was re-established.

About a week after this the patient suddenly began to develop signs of meningeal irritation, stiffness of the neck, a positive bilateral Kernig sign, and drowsiness. His temperature suddenly arose to 105 degrees. His coma deepened and he died on November 10, 1933. An autopsy of the brain was permitted. Gross and microscopical study of this organ and of the resected cæcum were reported by Dr. C. B. Courville of Los Angeles in part as follows:

"*Gross pathology.* The specimen consists of the dura mater covering the dorsolateral surfaces of the cerebral hemispheres, the entire brain and the cæcum, the latter being a surgical specimen. . . .

"*Brain.* The convolutions of the brain over the right hemisphere seemed to be somewhat universally flattened as compared to those of the opposite side. There were no particular areas, however, in which any unusual flattening was observed to point out the location of an underlying lesion. There has been in the recent state a fairly marked cortical congestion, and many of the smaller radicals are still visible even after embalming. The arteries are rather thin-walled throughout, although their tortuosity, especially over the cerebral cortex, would suggest that the patient was past middle age. The arachnoid shows considerable minor thickening and opacity in the region of the sylvian fissure, but not to the extent indicative of an inflammatory process.

"One rather interesting incidental finding is the extremely small size of the olfactory tracts, which are found as thin, string-like structures in the olfactory sulcus. There is a minor grooving of the uncinate region on either side and extends back particularly on the left to include a part of the hippocampal gyrus.

"There is a bilateral herniation of the cerebellar tonsils about the medulla in the region of the foramen magnum. There is also a marked herniation of the anterior two-thirds of the superior vermis and an adjacent triangular portion of the superior surface of the left cerebellar hemisphere through the tentorium. This herniation is undoubtedly due to the occurrence of a cerebellar lesion to be described later, and has taken place caudal to the brain stem.

"On the midpoint of the upper surface of the right cerebellar hemisphere adjacent to the vermis there is what appears to be a fluctuant area in this region, indicating its presence by loss of cortical markings, which measures 1.7 by 2 centimeters in its present state. The foliæ about this area are likewise considerably flattened and distorted.

"The cerebellum was cut in a horizontal section, passing through its anterior and posterior margins. This section reveals a fairly large encapsulated abscess in the upper part of the medial position of the right cerebellar hemisphere, extending into the adjacent vermis (Fig. 1). There is apparently the capsule of this abscess observed on the superior surface of the lobe. The abscess in its collapsed state measures 2.1 by 2.7 by 3.2 centimeters in its greatest transverse diameters. There is no evidence of loculation and diverticula from the main abscess cavity. The cavity is lined with a slightly uneven but well defined layer of greenish colored granular pus.

"There is next found a somewhat indistinct connective tissue capsule which varies between one-half and one millimeter in thickness. Outside of this a third layer is found consisting of a narrow, very well defined zone of reaction which is bright red in color and is evidently accompanied by considerable local congestion. The adjacent brain tissue seems to be remarkably well preserved. There is no evidence of rupture of this abscess. There is, however, considerable distortion and flattening of the fourth ventricle, which is reduced to a mere transverse slit. The dentate nucleus on the right is likewise compressed and distorted. There may be a slight œdema of the white substance of the right cerebellar lobe as compared with the left. The abscess seems to have occurred predominately in the narrow strip of white matter which radiates around the vermis toward the medial end of the posterior border of the lobe and has not disturbed the main centrum to any appreciable extent.

"The cerebral hemispheres were sectioned in a coronal fashion, beginning at the frontal lobes. The section which passes through the tips of the temporal lobes and just anterior to the genu of the corpus callosum reveals a slightly irregular contoured oval shaped cavity in the lower outer centrum of the right frontal lobe adjacent to the sylvian fissure. It is separated by a narrow zone of white substance 1.5 millimeters in thickness and by a very much attenuated and thinned cortex from the surface of the brain. The abscess cavity measures 2.2 by 2.5 by about 2 centimeters (anteroposterior diameter) in its greatest cross-sectional diameters (Fig. 2). The central portion of the cavity was filled with liquid, greenish yellow pus, while adjacent to the capsule there was a zone of more solid pus still of greenish color, but probably containing more fibrin. This pyogenic membrane can be separated from the capsule with a little difficulty, showing that organization of this portion had not occurred. The active connective tissue capsule must be very thin, for it was difficult to make out grossly, and probably in no place was it more than one-half a millimeter and often much less in thickness. Surrounding the capsule proper there is a brilliant reddish zone, evidently a zone of reaction in the surrounding tissues. This, however, is sharply circumscribed and within a millimeter or two outside this zone there is remarkably little evidence of any disturbance whatever. The white substance of this side shows only slight evidence of œdema, as suggested by a slight distortion of the midline structures.

"Further sections of the brain further indicate an œdema of the right frontoparietal centrum. Both lateral ventricles are dilated, probably due to the occlusion of the fourth ventricle. There is a slight distortion of the ventricular pattern with a minor deflection toward the left. This seems to be even more marked in succeeding sections where the third ventricle is found to be likewise markedly distorted and also deflected toward the left. The posterior horns are markedly dilated, and in this region the ependymal lining shows a number of small discrete petechial hæmorrhages. There seems to be no evidence of active inflammation in the ventricle.

"Smears from both abscess activities reveal numbers of tubercle bacilli.

"*Cæcum.* The colon specimen shows a large irregular yellowish gray mass in the region of the cæcum, which has invaded the bowel and caused an irregular ulceration. In this region the wall on cut section is found to be thickened, is very firm, and presents in some areas a whitish fibrous appearance, and in others a cartilaginous structure. In the outer portions of the mass there is more of a characteristic fibrous or fibrocaseous structure. As near as can be determined from the relationship of the appendix it seems as though the entire lower portion of the cæcum has been involved up to the base of the appendix. The wall of the appendix likewise seems to be thickened, firm and opaque in the upper two-thirds of its extent, and on cut section the tissue has a sort of gelatinous texture, so this organ has evidently partaken of the inflammatory process. The ulceration within the cæcum is very irregular and there is apparently a loss of epithelium down to the firm tumor tissue (Fig 3).

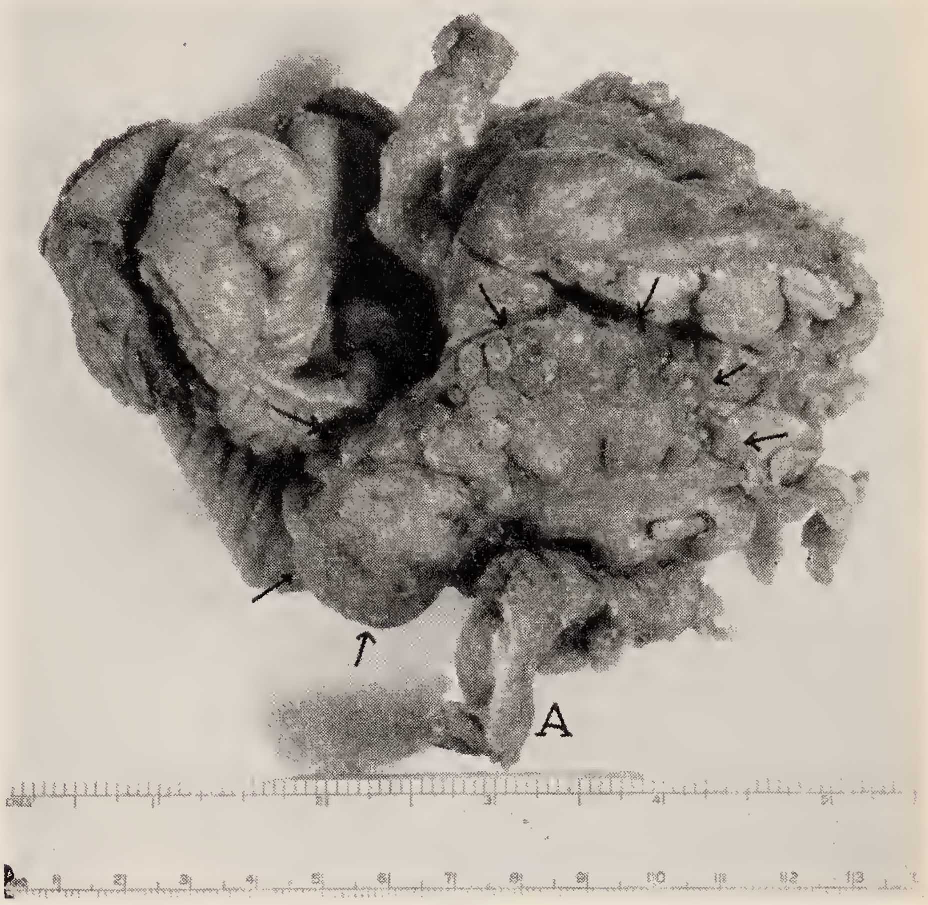

Fig. 3. Resected tuberculous mass including portions of colon, cæcum and appendix, *A*. The tuberculous mass is indicated by arrows.

"*Histopathology.* The following sections were taken from the abscess in the right frontal lobe:

"*Section 1, hæmatoxylin and eosin* (Fig. 4). The abscess wall was characterized by an irregular friable layer of wandering cells whose structure was not clearly made out, evidently having undergone a marked degree of degenerative change. There was next a thin wall of connective tissue also infiltrated with wandering cells. Just external to this wall the brain tissue was found to be œdematous and there was a certain increase in number of the interstitial cells. The overlying cortex had undergone a minor degree of œdematous change and was somewhat friable, but had undergone no gross arachnoidal change. The cells forming the exudate were examined under higher magnifications, but because of degenerative change their morphology was difficult to make out, however, many of them were obviously polymorphonuclear cells. There were also many mononuclear cells and some plasma cells observed. These cells could also be found in the connective tissue walls altho the mononuclear and plasma cells predominated.

"*Scharlack R for fat.* There was only a minimal amount of fat in the pyogenic layer, but outside of the wall were found numerous fat laden phagocytes, more abundant in some sections than others, and inclined to be scattered thru the tissue.

"*Section 2. Stain for tubercle organisms, Ziehl-Nielsen* (Fig. 5). Examination of the section under oil immersion reveals a large number of beaded or granular organisms both in the exudate and in the inner portions of the capsule of the abscess. These disappeared as the outer portion of the capsule was approached, so that none was found in the adjacent brain tissue.

"*Gram-Wiegert stain.* This method was used to determine whether or not other organisms might be present. It showed a number of 'beaded' or granular bacilli which seemed to be enclosed in capsules. These organisms were Gram positive and were probably tubercle bacilli. Smaller forms which were rounded, resembling diplococci, were also observed, which were probably small forms of the same organisms.

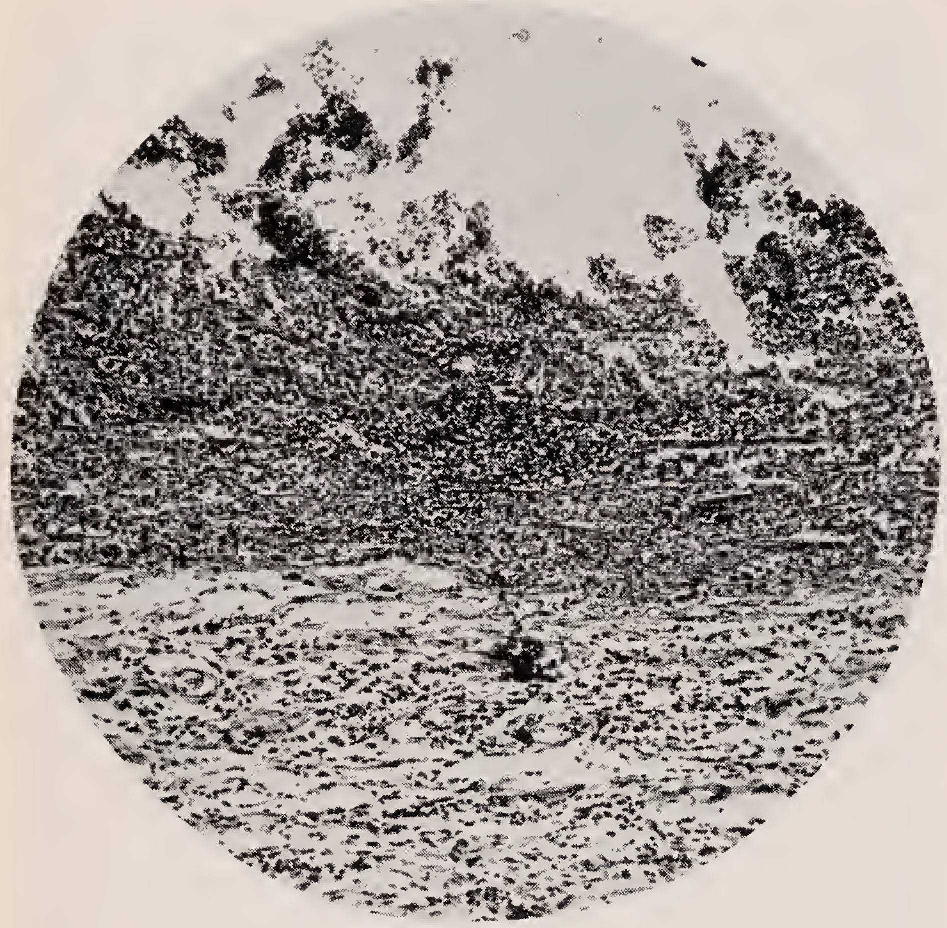

Fig. 4. Section of wall of frontal lobe abscess showing inflammatory reaction and connective tissue formation of capsule. No tubercles are present. Hæmatoxylin and eosin method. ×80.

"*Reticulum stain.* This section shows a rather condensed capsule of rather uniform size. There is a slight tendency to a fibrosis of the pyogenic layer, the processes extending from the walls of local blood vessels, which at times seem to be increased in number. There is also an evident increase in number of blood vessels in some portions of the brain, from which a beginning fibrosis is taking place.

"*Section 3. Gold sublimate method.* This method reveals some tendency to a proliferation of the astrocytes, but rather peculiarly at a distance from the wall of the abscess proper. These cells are predominant in a layer just beneath the cortex, while the intervening brain tissue between this zone of gliosis and the abscess wall is occupied by a cell which has undergone a degree of regressive change. This differs somewhat from the usual abscess in which an active proliferation of these cells is to be found immediately outside of the connective tissue wall.

"*Cajal's reduced silver method.* This method reveals nothing further of importance.

"*Section from margin of tuberculous mass in cæcum. Hæmatoxylin and eosin* (Fig. 6). The section is taken from the margin of the mass in the cæcum so that normal tissue could be found to compare with the abnormal. This is also taken with the purpose in mind of observing transitional stages of the process. Even in what appears to be normal tissue grossly at the margin of the mass are observed small tubercles of characteristic structure and containing typical giant cells. These tubercles are found predominantly in the submucous but at times are also observed in the muscular coats as well, particularly in the superficial portions. In the muscle layer and in the subserous tissues are found collections of lymphocytes with small hæmorrhages about the blood vessels. As one approaches the involved area there is a gradual replacement of the normal tissues with tuberculous tissue. The muscle coat is broken up and replaced with fibrous tissue, a reticular tissue, or with typical tubercles, which may be conglomerate. The subserous and epithelial layers are quite abruptly replaced with tuberculous tissue which at first diffusely invades the normal lymphoid tissue or replaces it with discrete tubercles. The lymphoid tissue becomes less and less conspicuous until finally there remains only small lymphocytic infiltration accompanying the pathological process. The glands seem to terminate quite abruptly for a short space; however, their remains can be identified by

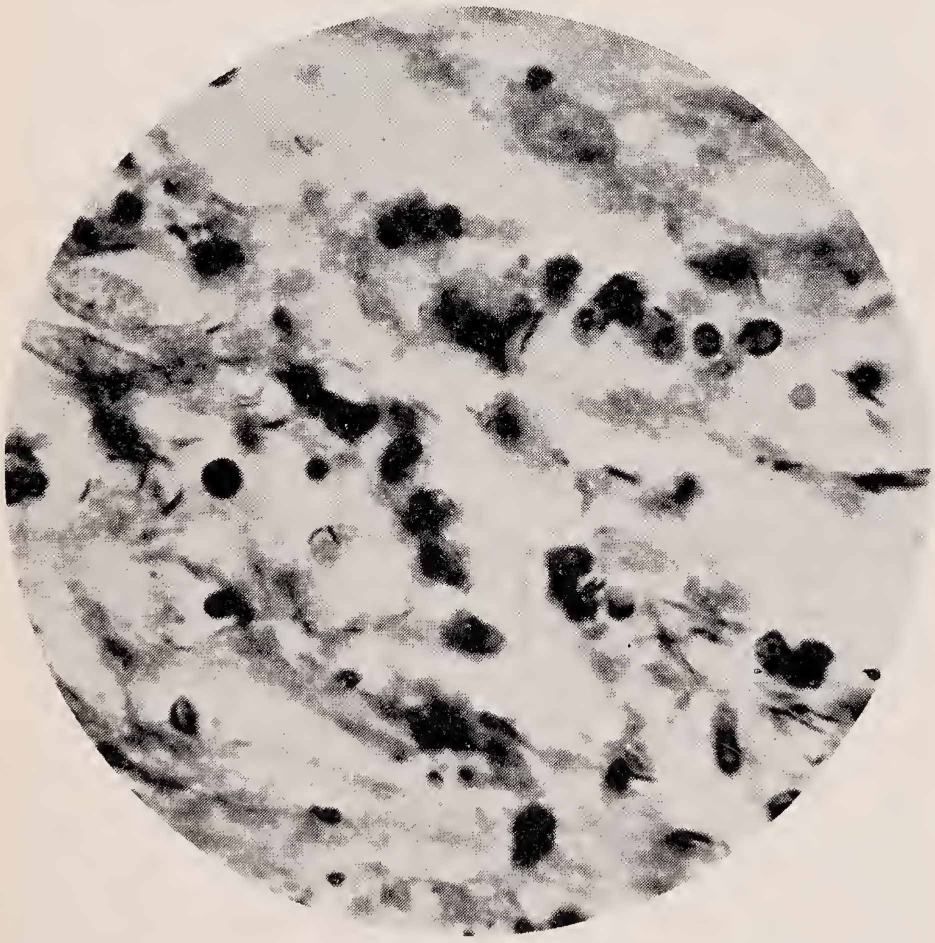

Fig. 5. Section of abscess wall right frontal lobe showing numerous tubercle bacilli scattered through the capsule. Ziehl-Nielsen method. ×900.

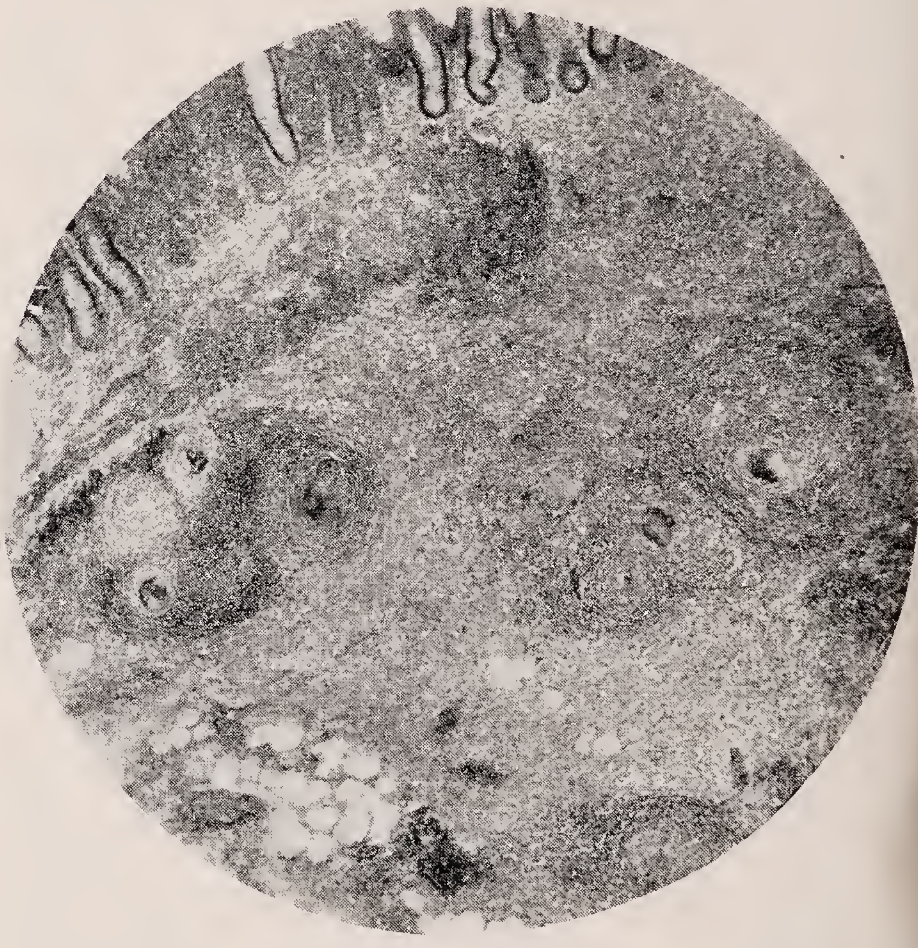

Fig. 6. Numerous conglomerate tubercles shown in submucous coat of cæcum. This process is quite different from that shown in the brain abscess of the frontal lobe. Hæmatoxylin and eosin method. ×36.

elongated spaces filled with red blood cells. In the margin of this tuberculous mass only an occasional gland can be made out. The characteristics of the abnormal tissue are typical fibroblasts, lymphocytes, plasma cells and giant cells forming typical tubercles or a more diffuse new formed tissue.

"*Diagnosis.* Tuberculous abscess of the right frontal lobe."

It is difficult to find, in the literature, reports of proved tuberculous abscess of the brain.

MacEwen (1893) discusses the possibility of abscess of the brain as a complication of tubercular disease of the middle and inner ear. He mentions the fact that there may be extensive tubercular destruction of the osseous walls, a condition which I believe is rarely seen today. When abscess occurs in such cases it is usually superficial, communicating with the middle ear often by minute passage through the granulation tissue. MacEwen states: "Instead of a distinct abscess in the midst of the cerebral tissues, a superficial cerebral ulceration is occasionally found in connection with tubercle of the middle ear, the pus from this ulceration being confined by the soldering of the meninges at the periphery of the ulceration to the base of the brain and the dura respectively. Such a purulent collection might thus appear as a localized cerebral abscess, the pus being retained between the brain which formed the dome, and the dura which formed the floor of the abscess cavity." In his series of 25 brain abscesses there was no case of true tuberculous abscess located in the substance of the brain.

Oppenheim (1911) mentions the fact that "in rare cases the *tubercle bacillus* has been found in the internal wall of the granular tissue lining the abscess, and in the pus itself (A. Fraenkel)." He goes on to state that he himself has found the tubercle bacillus in such an abscess during operation.

Reik (1910) reports a case of cerebral tuberculosis following otitis media in a 3½ year old colored boy, which was probably not a true tuberculous abscess in the sense we have defined it. The case, the report of which is well illustrated, shows the left temporosphenoidal lobe to be almost entirely involved in the process. The disease had extended from the middle ear, solitary tubercles being found in the dura at autopsy and large areas of tuberculous caseation being present in the temporal and parietal lobes. This caseation caused considerable destruction of both the gray and white matter, but was not surrounded by a true abscess wall.

Schorstein, in the Schorstein lecture of 1909, comments upon the rarity of tuberculous cerebral abscess secondary to tuberculosis of the lungs. He cites Gowers (1888) as stating that cerebral abscess never occurs when true tuberculous cavities are present in the lungs. However, this is not necessarily true, as Rudolph Meyer (1867) mentions one case of abscess of the brain with coexisting tuberculosis of the lungs. Again Finlay (1886) quotes a case of Dr. Hadden's of tuberculous pyopneumothorax with abscesses in the frontal and occipital lobes of the brain. Likewise he mentions one case recorded by Huguenin (1878). Fraenkel's case is again mentioned, and one recorded by Wernicke and Hahn where an abscess in the left occipital lobe was drained by trephining. The patient survived for 13 days and at postmortem examination tubercules were found about the abscess cavity. Fraenkel was of the opinion that there was a definite connection between the cerebral abscess and tuberculosis of the lung. Schorstein comments upon the fact of the very great infrequency of tuberculous cerebral abscess in association with pulmonary tuberculosis, calling attention to the relative frequency of brain abscess in connection with bronchiectasis: "Cerebral signs in tuberculosis of the lungs point almost invariably to tubercular meningitis. Cerebral signs in bronchiectasis mean in nearly every instance cerebral abscess."

In discussing the etiology of brain abscesses in general, Gowers (6) again (1898) states: "The last local cause (extremely rare) is a tubercular growth in the brain, which has been known to break down into a collection of pus. Other tubercular tumours and other evidence of tubercle are usually present, and indicate the origin of the abscess." The tuberculous process which he describes is the more common finding and is different from the pathology which we are discussing.

Hassin (1915) reports a case of multiple tuberculous brain abscess associated with dementia. The abscesses, however, "had no capsules and were separated from the cortex by an area of seemingly normal white substance. The abscess cavities were filled with a pea-green to yellow colored pus of a very offensive odor." Cultures and smears made from this pus were sterile; the diagnosis of tuberculous abscess being based upon the fact that the patient had "a chronic ulcerative and miliary tuberculosis of the lungs, combined with tuberculous osteomyelitis of sternum."

Adams (1896) under the title of "Tuberculous Abscess of the Brain" reports a case of a 10 year old colored boy who died of miliary tuberculosis. The right half of the brain contained many nodular masses which were probably miliary tubercles or tuberculomata of various sizes. In the center of these masses was an abscess mass 2½ by 2 by 1½ inches which contained "yellowish, turbid liquid within ragged cheesy walls." These were in the right frontal lobe. The pathologist reports that the tumors in the boy's brain showed only a few giant cells, the greater part of the mass being without any recognizable structure.

Leontine (1929) reports the case of a 27 year old man with a far advanced pulmonary tuberculosis. The sputum was positive, the lungs extensively involved, a tuberculous colitis was present, and a tuberculous meningitis suspected. At autopsy a tuberculous area in the parietal bone, which had caused extensive erosion, was found. The brain presented a large caseous area of tuberculosis which was apparently not a true abscess although it was so described in the title of the article.

Evans and Smith (1931) reported a case in a 14 year old girl who had an extensive scrofula of the neck of 8 years' duration. This patient had daily convulsions of increasing severity for 3 weeks and a terminal hemiplegia. The spinal fluid examination, 2 months before death, showed a clear colorless fluid containing 9 cells—all of which were lymphocytes—trace of albumin and globulin, a negative Kahn reaction, and a delayed positive reaction in testing for sugar by Benedict's method. Bacteriological examination and guinea-pig examinations were negative for tubercle bacilli. Another spinal fluid examination 3 weeks before death showed increased pressure, 8 cells, positive albumin and globulin, bacteriological examination was negative. Before death the child developed choking of the discs, mental torpor, and incoherence in speech. Autopsy showed a large abscess in the left frontal lobe which contained thick greenish pus, the examination of which revealed "abundant tubercle bacilli with typical morphology." There was no evidence of general meningitis. The pus was stained by Gram's method but no organisms other than tubercle bacilli were found. The region of the abscess was described as follows: "The outer layer of brain tissue showed practically no important changes with the exception of slight œdema. Bordering upon the necrotic area, there was noted a circumferential proliferation of connective tissue cells. There was likewise noted a number of new capillaries lying among the fibroblasts. These young capillaries were congested. The central area was composed of necrotic tissue, leucocytes, and lymphocytes."

Among the cases mentioned, apparently that of Evans and Smith is the only one of an undisputed tuberculous abscess. The gross illustration of their case is identical in appearance with ours. The process of formation is apparently the same as that of an ordinary pyogenic abscess. These authors found tubercle bacilli in large numbers in the pus, but did not try to identify them in the abscess wall. Such cases are not necessarily fatal, for Naffziger has cured one such case by drainage.

SUMMARY AND CONCLUSION

A case of multiple tuberculous abscesses of the brain is reported. This is believed to represent a rare type of tuberculous reaction in nerve tissue. The usual granulomatous or tubercle formation is not present. The abscesses apparently are formed as any other pyogenic abscess of blood-borne origin are. These tuberculous abscesses, when present, almost invariably accompany some other chronic tuberculous process in the body such as scrofula, tuberculosis of the cæcum or tuberculous mastoiditis. In the case here presented typical tubercle formation was present in the cæcum, but was absent in the walls of the cerebral abscesses.

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